Early Journal Content on JSTOR, Free to Anyone in the World

This article is one of nearly 500,000 scholarly works digitized and made freely available to everyone in the world by JSTOR.

Known as the Early Journal Content, this set of works include research articles, news, letters, and other writings published in more than 200 of the oldest leading academic journals. The works date from the mid-seventeenth to the early twentieth centuries.

We encourage people to read and share the Early Journal Content openly and to tell others that this resource exists. People may post this content online or redistribute in any way for non-commercial purposes.

Read more about Early Journal Content at http://about.jstor.org/participate-jstor/individuals/early-journal-content.

JSTOR is a digital library of academic journals, books, and primary source objects. JSTOR helps people discover, use, and build upon a wide range of content through a powerful research and teaching platform, and preserves this content for future generations. JSTOR is part of ITHAKA, a not-for-profit organization that also includes Ithaka S+R and Portico. For more information about JSTOR, please contact support@jstor.org.

AN EXPERIMENTAL STUDY OF JOINT AFFECTIONS INDUCED BY THE TYPHOID BACILLUS.*

A. G. ELLIS.

Associate in Pathology and Corinna Borden Keen Research Fellow of the Jefferson Medical College.

(From the Laboratories of the Jefferson Medical College Hospital, Philadelphia.)

AFFECTIONS of the joints, though not a rarity, are not excessively common during the course of typhoid fever. Despite their relative infrequency, certain clinical and pathological characters combine to render them of special interest. Among these points are the varied physical and bacteriological nature of the effusion, spontaneous dislocation, and the usually favorable, or at least non-fatal, course of the complication. This last fact largely accounts for our unsatisfactory knowledge concerning the pathology of these lesions.

Literature on both the clinical and experimental aspects of the subject is not conclusive. One point that was formerly disputed should now be regarded as definitely settled, namely, that the typhoid bacillus, even in the joints, is a pus-producing organism. This statement is not vitiated by the finding in some instances of sterile fluid in those cavities during the course of what clinically appeared to be a certain typhoid arthritis, as such finding is readily explained by experimental cases; the typhoid bacillus after producing the lesion dies out. Further, the cases in which the typhoid bacillus has been found in the pus of infected joints, although bacteriologic examination has too seldom been made, are sufficiently numerous to demonstrate the pyogenic properties of that organism.

Johnson[1] describes a case occurring in a woman of 25 years. During convalescence from typhoid fever her right wrist became swollen and painful. Pus aspirated from the joint contained a pure culture of the typhoid bacillus. Martin and Robertson[2] record a case in a man of 34. Pus aspirated from the fluctuating tumor about the wrist joint showed a pure culture of the typhoid bacillus. A second aspiration two weeks later showed only a small quantity of bloody pus.

Spontaneous dislocation of the hip is one of the most puzzling complications of typhoid fever. Ardisson[3] found that this disease was responsible for 33 of the 84 reported cases of this lesion; the other most frequent causes were polyarticular rheumatism with 23, and scarlet fever with 11 cases. Ardisson discusses at length the three leading theories of the cause of luxation, namely, (1) accumulation of fluid in the

---

* Received for publication January 20, 1909.

[1] *Ann. of Surg.*, 1900, 32, p. 135.

[2] *Montreal Med. Journal*, 1894, 23, p. 888.

[3] Thèse, Montpelier, 1903.

joint; (2) tissue proliferation in the acetabulum; and (3) the muscular theory. As before stated, this condition almost always terminates favorably and the pathology is therefore but little understood.

Graff[1] says that little is known of the mechanism of spontaneous luxation. Petit believed that an acute hydrarthrosis distended the capsule and ligaments. Verneuil and Reclus held that muscle pull plays a rôle and Hunter that the joint is dilated by an effusion of pus. From numerous Röntgen-ray studies of spontaneous dislocation after typhoid, puerperal sepsis, and acute osteomyelitis, Graff believes that in all cases the upper part of the acetabulum flattens, in part disappears, no actual destructive process, however, being demonstrable. The effusion in the joint is serofibrinous and without capsular dilatation leads to inflammatory softening of the upper acetabular rim. Pressure upon this by the head of the femur leads to atrophy and flattening so that the head slowly moves above and posterior.

Freeman[2] reports a case of spontaneous dislocation of the hip in a girl of 10 years. He says that most writers agree that the prime factor in dislocation is overdistension of the joint by fluid. The ligamentum teres is not necessarily ruptured, Moore having experimentally demonstrated that it may be sufficiently elongated by an intraarticular effusion to allow of complete dislocation without loss of continuity.

Kummer[3] says regarding the content of the joint in cases of spontaneous dislocation of the hip in connection with acute infectious diseases, that in 29 cases in which the presence of arthritis was known before dislocation occurred, 22 were serous or serofibrinous and three purulent. Kummer adds two typhoid cases of his own but does not give the bacteriology of any of the 51 cases of spontaneous dislocation of which he presents brief notes.

I have found but two reports that are at all definite upon the pathology of spontaneous dislocation, and one of these is valuable largely for its negative findings. Both were old operative cases and hence throw no light on the early stages of the joint affection.

Rawdon[4] describes a case occurring in a girl of eight years. He first saw the patient in June, the history being that during an attack of typhoid fever which lasted from February to May, she complained of pain in the right thigh and knee but not in the hip; later, deformity of the thigh developed. Rawdon operated, removing the head of the femur. The head showed no notable absorption. Synovial membrane was not demonstrable. The cartilage was in general intact, showing only a little absorption around the circumference at its junction with the neck. The bony structure of the head and neck was absolutely normal and the surrounding tissues were notably healthy.

Hübener[5] reports the case of a girl of 14 years, admitted to the hospital April 1. The preceding September she had an attack of typhoid fever with a short recurrence on the 31st day. Two months afterward the right hip became affected. The foot and knee previously swelled but soon subsided under treatment. Pain in the hip kept the child in bed for a time and then the hip was found to be out of joint. A skiagraph showed dislocation of the femur, the acetabulum being still well formed with a sharp border. The head of the femur was loose at the epiphyseal line. Operation revealed the acetabulum empty and covered by slight masses of granulation tissue. The head of the femur was free and lay behind and above the acetabulum imbedded in a moderate amount of granulation tissue. The head of the bone and the new tissue were removed. In this tissue were typhoid bacilli. The patient died but autopsy was not permitted. Hübener believes there was exudate in the joint before dislocation occurred.

---

[1] *Centralbl. f. Chir.*, 1901, 28, p. 1243.

[2] *Med. News*, 1895, p. 452.

[3] *Revue de Chir.*, 1898, 18, pp. 55, 111, 319, 632.

[4] *Liverpool Med. Chir. Jour.*, 1882, 2, p. 22.

[5] *Mitteil. a. d. Grenzegebiet. d. Med. u. Chir.*, 2, H. 5.

As with the clinical, so with the experimental studies of typhoid joint affections. But little work along this line has been done and the findings are therefore not conclusive. Investigations have been made chiefly upon rabbits, as, though those animals are quite refractory to the typhoid bacillus, they are in many ways the most suitable for experimental work.

Orloff[1] found that the effusion in joints after the injection of typhoid bacilli may be serous, seropurulent, or purulent, the first and second being most frequent. He injected 13 rabbits in the knee joint, at the same time injecting into the opposite joint sterile water or broth, according as he had employed an emulsion of agar growth or broth culture of the bacillus. One-half to one cubic centimeter of the material was used. The joints were studied after periods of time ranging from 15 hours to 37 days.

Twenty-four hours after injection the joints were swollen and the subcutaneous tissues edematous. In some instances the whole lower leg showed edema, this probably being partly due to the 5 per cent carbolic acid solution used to disinfect the leg. Removal of the skin during the first 12 to 24 hours revealed dilated vessels, this also being true of the synovial membrane; at times there was actual hemorrhage. In the cases investigated later the hemorrhage was slight. In the joints, especially the upper recess, was a thick, tough, more or less cloudy fluid not seldom in large quantities. Joints examined later contained opaque, white, moderately hard, kernel-like masses and the fluid was more turbid and seropurulent in type. In from 24 to 37 days the fluid was still more thick and adherent to the synovial membrane. In the fluid of the first day, also later, were pus cells in small or large numbers. Typhoid bacilli were present during the first two days; after eight or nine days they were with one exception absent; in that one instance they were found on the 13th day. In the control knees the injected fluid was entirely absorbed.

Orloff also injected typhoid bacilli into muscles, under periosteum, etc., in order to investigate the pus-producing properties of that organism. His résumé concerning the joint lesions was that there was produced a seropurulent, frequently thick, mucus-like exudate. He afterward repeated his experiments using sterilized cultures instead of living bacilli and obtained the same results, though the reaction was weaker. One of his conclusions was that the suppurative processes developing during typhoid fever, when the pus contains exclusively typhoid bacilli, are due to that organism alone and are not to be regarded as the consequence of a mixed infection of typhoid bacilli and pu-cocci.

Arcoles[2] injected broth cultures of the typhoid bacillus into joints or veins of five young rabbits. He produced suppurative arthritis by direct injection into joints or by injuring joints after injecting bacilli into a vein. Bacilli were found in the effusion in the affected joints.

[1] *Centralbl. f. Bakt.*, 1890, 8, p. 366.

[2] Abs. in *Centralbl. f. Chir.* 1898, p 266.

Florange[1] believes that typhoid arthritis comes often from lesion of the neighboring bone. The typhoid bacillus is constantly in the bone marrow of those suffering from typhoid fever and its pyogenic powers are well known. It may then invade a joint from the bone and thus be a propagation from an osseous infection. Most often, he believes, there is not a typhoid infection, properly so called, of the joint, but simply an irritation of the neighboring parts caused by an inflamed epiphysis; the articular effusion is sterile. The epiphyseal osteitis is here the principal lesion, the arthritis being secondary and less important. Florange's contention is partially supported by the experiments of Klemm,[2] who injected eight rabbits in an ear vein and afterward found in the bone marrow of five of them a pure culture of the typhoid bacillus, though arthritis was not induced. Pus was found in none of the cases.

My object in carrying out the experimental study here recorded was to add to our knowledge of the action of the typhoid bacillus in joints, especially, if possible, after causing their presence in those cavities by means other than direct injection.

The first set of experiments was made by using a broth growth of a stock culture of the typhoid bacillus of uncertain virulence. One c.c. of a 24, 48, 72-hour, or older, growth was injected directly into a knee joint and those structures examined at various periods later. In all of this series the skin over the site of injection was first washed with soap and water and then with a 5 per cent carbolic acid solution. When the joints were examined, spreads and inoculations were made from the joint content and in most instances tissue was fixed and finally studied in stained sections. The results can best be given in brief protocols of the individual animals. Spontaneous death as it occurred in some of the rabbits, with the exception of the one due to pneumonia, in these series of cases, was apparently due to the lesion produced or to the conditions of captivity; at least no anatomic changes pointing to other more definite causes were found.

RABBIT 1.—One c.c. 24-hour broth culture typhoid bacillus injected in knee joint. Next day joint red and much swollen, second day moderately swollen, third day essentially normal. (These early phenomena were common to all the animals of this series.) Rabbit chloroformed on seventh day. Joint moderately distended, motion less free than on opposite side. In joint is 0.5 c.c. thick, tenacious, grayish fluid. Synovial membrane lusterless. Microscopically, fluid contains numerous cells, 53 per cent polynuclear, 47 per cent mononuclear. Many of the latter are evidently endothelial cells and some of them contain polynuclear leukocytes in varied stages of disintegration. Sections through the cartilage of the femur show a covering of granular acidophilic detritus and leukocytes but no erosion. Inoculations from the joint were sterile.

RABBIT 2.—One c.c. 48-hour broth culture typhoid bacillus injected in knee joint. Animal killed on 10th day. Joint slightly swollen and motion less free. Practically no free fluid in joint cavity. Spreads from scrapings contain many cells, mononuclear 87 per cent, polynuclear 13 per cent. Tissues show no lesion. Inoculations from the joint remained sterile.

---

[1] Thèse de Paris, 1902.

[2] *Archiv f. klin. Chir.*, 1893, 46, p. 862.

RABBIT 3.—One c.c. 72-hour broth culture typhoid bacillus injected in knee joint. Animal found dead on 10th day, the joint having been gnawed open by other rabbits. In the spreads from the content are great numbers of cells, approximately 65 per cent mononuclear, though degeneration is too advanced for an accurate count. Synovial membrane shows engorgement of vessels and infiltration by mononuclear cells; no erosion.

RABBIT 4.—One c.c. 72-hour broth culture typhoid bacillus injected in knee joint. On second day an unsuccessful attempt was made to withdraw fluid from the joint by means of a hypodermic needle. Rabbit chloroformed on 58th day. No erosion of tissues. Inoculations gave growth of unidentified cocci.

RABBIT 5.—One c.c. six-day broth culture typhoid bacillus injected in knee joint. Rabbit found dead on 33rd day. Joint not swollen and contains small quantity of tenacious, almost clear fluid. Vessel around joint slightly injected. No erosions. In spreads a few cells, all mononuclear, well preserved. Inoculations sterile.

RABBIT 6.—One c.c. 48-hour broth culture typhoid bacillus injected in knee joint. Rabbit killed on fourth day. Joint is moderately swollen and motion less free than on opposite side. Interior of joint essentially the same as in Rabbit 1. Spreads contain many cells, 88 per cent of which are polynuclear. No erosions.

RABBIT 7.—One c.c. 48-hour broth culture typhoid bacillus injected in knee joint. Rabbit found dead on 16th day. Apparently only normal amount of synovial fluid within joint. Spreads contain very few cells, many so degenerated that accurate differential count cannot be made. Tissues of joint show no definite lesion. Inoculation sterile.

RABBIT 8.—One c.c. six-day broth culture typhoid bacillus injected in knee joint. Animal killed on 45th day. No evident gross lesions. Few cells in spreads, all mononuclear and well preserved. Tissues show no lesion. Inoculation from joint sterile.

RABBIT 9.—One c.c. 24-hour broth culture typhoid bacillus injected in knee joint after it was roughly manipulated for one minute. Rabbit found dead on sixth day. Considerable thick, grayish fluid in joint. Synovial membrane grayish. In spreads are many cells, polynuclears 72 per cent. Tissues show no lesions. Inoculation gave pure culture of typhoid bacillus.

RABBIT 10.—One c.c. 24-hour broth culture typhoid bacillus injected in knee joint. which was then scraped with point of needle. Rabbit found dead next day. No free fluid in joint but a scanty, tenacious, almost clear material adheres to synovial membrane. Latter structure ecchymotic where injured by needle. In spreads are enormous numbers of cells, 98 per cent polynuclears. Inoculation from joint gave pure culture of typhoid bacillus.

The results of these experiments indicated that the bacilli employed were not sufficiently virulent to produce noteworthy lesions in the joint tissues, although an inflammatory exudate appeared in the cavity. They did show that at first the cells in the exudate were practically all polynuclear leukocytes, these after a few days giving way to mononuclears. The latter were nearly all of the large or hyaline variety of lymphocyte or were endothelial cells, very few lymphoid cells being found. The endothelial cells were phagocytic for polynuclear leukocytes.

In the eight cases in which inoculations were made from the joint the typhoid bacillus was found twice, after the lapse of one and six days respectively. Five others were sterile at the end of 7, 10, 16, 33, and 45 days. One only, No. 4, contained bacteria other than the typhoid bacillus; the presence of cocci in this case is fully explained by the fact that on the second day an attempt was made to aspirate the joint.

In the second series of experiments, the typhoid bacilli employed were increased in virulence by repeated passage through guinea-pigs until one-tenth loop intraperitoneally was sufficient to kill a 200-gram pig within 18 hours. Emulsions of 24-hour agar growth in sterile water were used for injection. In order to avoid the irritating effect of carbolic acid solution, the skin over the joint was prepared by simply washing with alcohol. That this was sufficient precaution is shown by the fact that contamination not once occurred, inoculations from the joints always giving a pure culture of the typhoid bacillus or remaining sterile. The typhoid bacillus was identified during its preparation and in the cultures from joints by the fermentation, Conradi-Drigalski, and agglutination tests.

I began this series with the attempt to induce lesions of joints in some way other than by direct injection into them of bacilli. With this aim several methods were employed only to be abandoned because of anatomic or operative difficulties or because of lack of results. The 10 experiments in this group are as follows:

RABBIT 11.—One-tenth loop typhoid bacilli injected into left carotid artery and double ligature applied. Animal died in 13 days from double pneumonia and pleuritis. No joint lesions.

RABBIT 12.—Injected same as No. 11. Rabbit apparently sound at end of 57 days.

With several rabbits attempts were made, after the injection of bacilli into the circulation, to create by trauma or by interference with the circulation a *locus minoris resistentiae* in one or more of the joints, with the hope that in this way the bacilli might be induced to colonize therein. This object was not attained. In one animal a fruitless attempt was then made to throw the bacilli into the circulation at a site nearer the joint than is the ear.

The idea of causing localization of bacilli in joints by way of the circulation was then abandoned and the remainder of the experiments confined to injecting bacilli directly into the joints. To produce a condition comparable to that in human beings with typhoid fever, if the bacilli lived, injections were made into the veins of four rabbits at different periods before the joints were inoculated.

RABBIT 13.—One-tenth loop typhoid bacilli injected into ear vein. One week later one loop bacilli injected into knee joint. On following day the joint was red and greatly swollen. Animal killed on seventh day when nearly dead. The injected joint was loose, that is, permitted unusual latitude of motion especially in the lateral direction. In the joint was a small quantity of soft, yellowish, granular material. This was in connection by small openings through the capsule with two periarthritic abscesses. Spreads of the joint content show many endothelial cells, most of which contain numerous vacuoles. In addition are enormous numbers of leukocytes, at least three-fourths of which appear to be polynuclear though many are so degenerated that their type cannot be determined. A few threads of fibrin are present. Inoculation from the joint remained sterile.

RABBIT 14.—Injected in ear and joint same as No. 13. Animal killed on eighth day when nearly dead. Injected joint very loose, can be fully flexed readily and bent laterally to angle of 50 degrees. The quadriceps tendon can easily be thrown out of its groove by manipulating the joint; this cannot be done with the opposite leg. In the joint is a considerable quantity of yellow, moderately tenacious fluid. Over the surfaces of the joint and extending upward for some distance in the sheath of the quadriceps tendon is a yellowish, friable deposit resembling degenerated fibrin. In the posterior recess of the joint is 1 c.c. of thick, yellow pus.

The interarticular ligaments are destroyed, remaining only as indefinite masses of reddish-yellow débris covered by the described exudate. The semilunar and articular cartilages are not appreciably affected, either in color or consistency. In spreads from the joint content are many leukocytes, 95 per cent of which are polynuclears. In many only the nucleus remains. There is a moderate number of endothelial cells, with more or less fatty degeneration of the protoplasm. Inoculations from the joint gave a pure culture of the typhoid bacillus.

RABBIT 15.—One-tenth loop typhoid bacilli injected in ear vein and four days later one loop in third joint of hind leg. Animal found dead on 13th day. Pronounced serofibrinous pleuritis and pericarditis. Joint contains small quantity of tenacious, turbid fluid, in which are endothelial cells and moderate number of leukocytes, about half of the latter polynuclears.

RABBIT 16.—One-tenth loop typhoid bacilli injected in ear vein and three days later one loop in third joint of hind leg. Animal found dead on 47th day, the joint differing in no wise from the corresponding one on the opposite side.

The results in Rabbits 13 and 14 show clearly that a suppurative arthritis can be induced by the typhoid bacillus. Further, and this is of special importance in connection with the problem of spontaneous luxation, is the fact that motion in the affected joints was of much greater latitude than is normal. This in No. 14 is readily explained by the destruction of the interarticular ligaments; in the other, changes in the capsule and surrounding tissues, with possibly some yielding of the ligaments, must be held accountable. That a suppurative arthritis is present as the underlying lesion in all, or even any, of the cases of spontaneous luxation in human beings cannot be said; in truth, the clinical history of most of them would indicate that such was not the case. Notwithstanding this, the fact that the typhoid bacillus can occasion such destruction of articular tissues as was found in Case 14 is of importance. This case is further of interest in that the typhoid bacillus was still living in the joint on the eighth day after injection.

In the remaining experiments of this series, typhoid bacilli were injected directly into the knee joint, this being the only expedient employed.

RABBIT 17.— One-half loop typhoid bacilli injected in knee joint about 4 P.M. Animal found dead next morning with no evidence of reaction in the joint. Spreads from the joint content contain numerous bacilli and occasional endothelial cells. Inoculation from the joint gave a pure culture of the typhoid bacillus.

RABBIT 18.—One loop typhoid bacilli injected in knee joint. Next day, joint red and greatly swollen. Animal killed on fourth day. Joint much swollen, containing a thick, tenacious, yellow fluid. In spreads are many cells, 93 per cent polynuclears, most of remainder endothelial cells. Many of both types show extensive degenerative changes. A few of the polynuclears contain bacilli. The joint tissues show no erosion. Inoculation from joint gave pure culture of the typhoid bacillus.

RABBIT 19.—One-half loop typhoid bacilli injected in knee joint. Next day, joint red, swollen, and tender. Third day rabbit sick, with profuse diarrhea. On sixth day was emaciated but fairly lively; was killed. In the swollen joint is considerable turbid fluid. This is especially true of the posterior part from which a mass of cheesy material extends into the surrounding tissues. Articular surfaces and ligaments show no gross lesion. Spreads contain enormous numbers of leukocytes, 95 per cent polynuclears, and many endothelial cells, the latter showing extensive fatty degeneration. Inoculation from joint proved sterile.

A piece of the muscle bordering the joint was prepared and sectioned. Sections including the joint capsule and attached tissue show on the former a mass of exudate consisting of leukocytes, fibrin, and red cells. A few endothelial cells are also present. The outer portions are thickly infiltrated by mononuclear cells, chiefly large with vesicular nuclei, among which are a few polynuclears. The muscle has for the larger part almost or entirely lost its cross striation. The fibers are in many instances partially hyaline and show pronounced longitudinal furrowing or actual separation into fibrils. At points the blood vessels are surrounded by mantles of mononuclear cells.

RABBIT 20.—One loop typhoid bacilli injected in knee joint. Next day joint much swollen and red. Animal found dead on eighth day, the joint being greatly swollen. In it is a large quantity of thick, yellow fluid exactly resembling pus as found in human beings. This permeates the entire joint, being beneath the semilunar cartilages. Adherent to the articular surfaces is a quite thick layer of grayish-yellow material undoubtedly fibrinous in character. The interarticular ligaments are covered by the exudate and the superficial portions are necrotic. The periarticular tissues are also infiltrated by pus. The articular cartilages are not eroded. Spreads from the joint content contain a great deal of fibrin and numerous leukocytes, many of which show pronounced degeneration; the great majority of those still identifiable are polynuclears. A few degenerated endothelial cells are present, as are also occasional bacilli. Inoculation from the joint contents, though only a few colonies grew, proved a pure culture of the typhoid bacillus.

Portions of the quadriceps tendon and of the adjoining muscle were fixed and sectioned. Microscopically the muscle is largely necrotic, these areas being closely packed with leukocytes. Most of these are polynuclears, though bordering the necrotic masses mononuclears predominate. The outlying portions of muscles not yet necrotic have lost their transverse striation. Between the fibers are many mononuclear cells and also numerous polynuclear eosinophiles. The inner surface of the tendon is also partly necrotic. In the remainder the fibers are separated by mononuclear leukocytes and here, as in the muscle, are polynuclear eosinophiles.

RABBIT 21.—One-half loop typhoid bacilli injected in knee joint which became red, swollen, and tender. Animal found dead on eighth day. The joint is swollen but its motion not freer than that of the one opposite. In the joint is a small quantity of thick, yellow fluid, which in the posterior pocket becomes caseous. The anterior interarticular ligament is covered by exudate and the superficial portion is slightly necrotic. Just posterior to the insertion of this ligament on the tibia is an area of erosion 2 mm. in diameter, in which jagged bone is exposed.[1] Spreads of the joint content contain many leukocytes, a large number degenerated but the great majority polynuclear. Endothelial cells, some showing fatty degeneration, are also present. Inoculations were not made.

Sections through the joint capsule and adherent tissues are densely infiltrated by mononuclear cells, many with large, partly vesicular nuclei. At points are masses of fibrin. The quadriceps muscle shows distention of blood vessels, collection of mononuclear leukocytes in the interstitial tissue, and hyaline degeneration of some of the fibers.

RABBIT 22.—One-half loop typhoid bacilli injected in knee joint which became red, swollen, and tender. Animal found dead on eighth day. The joint is very loose, especially permitting excessive lateral motion. In the joint is a large amount of grayish-yellow fluid. The anterior interarticular ligament is reduced to a few threadlike masses of reddish material covered by exudate. The internal borders of the semilunar cartilages are eroded and thinned; the articular cartilages are intact. Spreads of the joint fluid contain many leukocytes, 95 per cent polynuclears, showing but little degeneration, a moderate number of fatty endothelial cells, and numerous threads of fibrin. Inoculations were not made. Sections from the quadriceps muscle show extensive infiltration by mononuclear leukocytes, particularly in the vicinity of vessels. The muscle shows pronounced granular degeneration.

---

[1] Bone from this and other cases in which that structure was involved, or at least kept for investigation, was accidentally destroyed by fire and therefore microscopic studies of it could not be made.

RABBIT 23.—One-third loop typhoid bacilli injected in knee joint. Animal found dead on eighth day. Joint is swollen but not loose. In the joint is yellowish-gray exudate. The capsule anteriorly and the quadriceps muscle extending over and along the tendon are largely necrotic. The interarticular ligaments are covered by exudate but not otherwise appreciably affected. Spreads show essentially the same as in No. 22. Inoculation from joint sterile. Sections through the quadriceps muscle well above the exudate show at the tendon insertion a perivascular round-cell infiltration. Many of the fibers have lost their transverse striation and stain less deeply than do those of normal muscle.

RABBIT 24.—One-third loop typhoid bacilli injected in knee joint. Animal found dead on 10th day. In the greatly swollen joint is a large quantity of yellowish exudate. The interarticular ligaments, semilunar and articular cartilages show no gross lesions. In spreads of the exudate is a great deal of fibrin. The cells, though both poly- and mononuclear can be recognized, are too much degenerated to permit definite statements regarding their percentages. Inoculation from the joint gave a pure culture of the typhoid bacillus.

RABBIT 25.—One-third loop typhoid bacilli injected in knee joint. Animal found dead on 11th day. The joint is moderately swollen. Vessels of fascia around and for some distance above the joint are markedly injected. The joint capsule is also injected and at points anteriorly is much softened and easily torn. In the joint is a small quantity of yellowish fluid and in the posterior recess a collection of yellow, granular material. There is no erosion of ligaments or cartilages. In spreads of the joint fluid is a moderate number of leukocytes, many degenerated, the majority present being polynuclears. Inoculations from the joint gave a pure culture of the typhoid bacillus. Sections from the quadriceps muscle show slight granular degeneration of that structure.

RABBIT 26.—One loop typhoid bacilli injected in knee joint. Animal killed on 12th day. In the joint, which permits freer motion than that on the opposite side, is a small quantity of yellow, tenacious material. Extending into the surrounding tissues from posterior portion of joint is a cavity containing 1 c.c. thick yellow pus. In spreads of the joint fluid are a great number of leukocytes most of which are markedly degenerated but the majority are polynuclear in type. Inoculations from the joint proved sterile.

Sections from the muscles bounding the joint show in areas atrophy but most prominent is hyaline degeneration which here is very extensive. Entire fibers, in some instances several adjoining ones, have lost all structure and appear as a hyaline material staining very slightly by eosin. Such areas are widespread through the sections. Small areas of necrosis are also present, confined to the fibers alone. Some of the necrotic material stains very deeply by hematoxylin, suggesting the probability of calcareous deposits. Between these necrotic muscle fibers the interstitial tissue is very densely infiltrated by leukocytes, the majority mononuclear. In some of the sections the hyaline degeneration is very prominent and necrosis and leukocytic infiltration slight or entirely lacking.

RABBIT 27.—One-third loop typhoid bacilli injected in knee joint. Animal found dead on 14th day. Joint swollen with yellow discoloration above and below. The capsule is grayish-yellow and soft. In the joint is a small quantity of yellowish fluid with considerable granular material in the posterior part. The interarticular ligaments are covered with exudate but not eroded. Spreads of the joint fluid contain many degenerated leukocytes, a few endothelial cells, and threads of fibrin. Inoculations from the joint were sterile.

RABBIT 28.—One-third loop typhoid bacilli injected in knee joint. Animal found dead on 14th day. In the greatly swollen joint is a small quantity of yellow, tenacious fluid. Between the interarticular ligaments and extending laterally, the head of the tibia is bared and eroded over an area 0.5 cm. in diameter, presenting a rough, spiculated surface. The capsule is partly necrotic; the interarticular ligaments and joint cartilages are not eroded. Spreads from the joint fluid contain many leukocytes, a few fibrin threads, and a number of greatly degenerated endothelial cells. Inoculations from the joint were sterile. Sections of the muscles bordering the joint show necrosis and leukocytic infiltration as described under No. 26.

RABBIT 29.—One loop typhoid bacilli injected in knee joint. Animal found dead on 16th day. In the swollen joint is a moderate quantity of quite thick, yellow fluid. Beneath the semilunar cartilages is a thin layer of fibrinous exudate. In the middle of the head of the tibia, extending from the anterior margin to the interarticular ligament and to a small extent over the articular surfaces, is an almost circular area 1 cm. in diameter in which the bone is bared of its covering and is carious and jagged. From this point the anterior portion of the capsular ligament is necrotic and opens into an abscess which extends under the tendon and to the surrounding tissues. The capsule is also destroyed posteriorly and the joint cavity here connects with the surrounding abscess. On one of the articular facets of the femur the articular cartilage is superficially eroded over an area 3 by 8 mm. in extent. In spreads from the joint content are a few partly degenerated endothelial cells and an enormous number of leukocytes, 90 per cent of which are still recognizable as polynuclears. Inoculations from the joint proved sterile.

SUMMARY OF THE RESULTS IN THE 13 RABBITS, NOS. 17 TO 29 INCLUSIVE, IN WHICH DIRECT INJECTION OF TYPHOID BACILLI INTO A JOINT WAS THE METHOD EMPLOYED.

In all of the 12 animals which survived a sufficient length of time, a seropurulent or purulent exudate appeared in the joint. In three instances there was more or less extensive necrosis of interarticular ligaments. In one there was erosion of the semilunar cartilages. In three cases there was destruction of the overlying soft parts and erosion of the articular surface of bone, in each instance the head of the tibia being affected. In three cases the muscles bordering the joint showed hyaline degeneration, accompanied or not by areas of necrosis. Inoculations were made from the joint content in 11 of the 13 cases. The typhoid bacillus in pure culture was recovered in five instances, after the lapse of 1, 4, 8, 10, and 11 days respectively. The exudate was sterile in six cases, at the end of 6, 8, 12, 14, 14, and 16 days.

In order to verify Orloff's findings as regards the effect of dead bacilli in the joint, I used this material in two experiments. The source of the bacilli employed was guinea-pig 19, the same as that of the organism employed for many of the knee injections already described, hence of equal virulence. The suspension of bacilli was placed before injection for one hour in an oven at 60°C.; inoculations made from this suspension at the time of injection proved it to be sterile.

RABBIT 30.—One loop typhoid bacilli killed by heating for one hour at 60° C. injected in knee joint. Next day the joint was red, swollen, and tender. Second day less swollen, third day normal in size and color. Animal found dead on the eighth day. The injected joint microscopically is exactly like the corresponding one of the opposite side. Spreads from the fluid contain a few well-preserved endothelial cells.

RABBIT 31.—Injected same as No. 30. Next day the joint was red, swollen almost as much as those in which living bacilli were used, and tender. Second day was less swollen, third day normal in appearance. Animal found dead on 25th day. Knee joints on the two sides absolutely alike.

These two experiments are of course insufficient upon which to base conclusions but the results in my cases are so opposed to those of Orloff as to be noteworthy. He obtained the same effect, except in lesser degree, from killed as from living bacteria. What my two animals would have shown had the joints been examined during the quite violent, but temporary, reaction of the first day or two after the injection is problematical, but Orloff's statement was based on a comparison with his other series which included periods of time up to 37 days.

Since cases of spontaneous luxation as a feature of typhoid joint affections in human beings are limited to the hip, I attempted finally, for the sake of better comparison, to induce lesions in that joint, instead of in the knee, in rabbits.

RABBITS 32 TO 38 INCLUSIVE.—Attempted injection of typhoid bacilli into hip joint. Owing to the depth of the joint and its anatomical structure, the capsule was not penetrated by the needle in any of the seven cases. The bacilli were deposited in the tissues overlying the joint or in the neighboring muscles.

These animals all died in from 4 to 14 days, presumably from the effects of abscesses or local necroses which developed at the site of injection. The muscles bordering these lesions show in stained sections hyaline degeneration and necrosis as already described in connection with a number of the knee cases. In one instance, in addition to these lesions, the bordering muscle shows quite marked increase of connective tissue, amounting to a distinct productive interstitial myositis.

In general the experiments described in this paper show clearly that the typhoid bacillus is capable of seriously damaging and even destroying the various elements entering into the formation of joints. Collectively, all the component parts of those structures—synovial membrane, interarticular ligaments, semilunar cartilages, articular cartilages, bone, the joint capsule—and the surrounding tissues, including the muscle, were thus affected. Certain of these points, to the best of my knowledge, had not previously been demonstrated and they consequently throw some light on those phases of the pathology of this affection.

Just how far it is safe to apply these findings in animals to the interpretation of typhoid joint affections in human beings is difficult to say. I believe we are justified in considering that all the destructive effects here enumerated are at least possible in human joints. There at once arises the objection that the bacilli experimentally were injected directly into the joints while in man they enter those structures, if they are present, directly or indirectly by way of the blood stream. This however, I think, is not an insuperable objection. When the bacillus colonizes and multiplies in the joint its effects must be much the same whatever the portal of entry, providing of course that preceding trauma does not play too large a rôle. While trauma is inflicted by injection in experimental work, the puncturing of the capsule by a fine needle is not a great injury. As before stated, contamination by other bacteria did not occur in a single instance of simple injection.

My study adds but little that is definite concerning our knowledge of spontaneous dislocation, as this complication did not occur in any of the experiments. In truth, reasoning from the cases in man, it was not to be expected, since attempts to produce infection of the hip joint were not successful. Generally speaking, the results show how dislocation would be favored by the partial or entire destruction of interarticular ligaments and the joint capsule. In one case, No. 14, these structural changes permitted such excessive motion in the joint that dislocation was not at all a remote possibility.

Finally, the outcome of this study suggests at least two points that might be worthy of consideration in further research upon the subject. First, the employment of larger animals, as hares or even monkeys, in which bacilli could be introduced directly into arteries near the joints. Second, the preparation of typhoid bacilli by growth upon culture media to which was added increasing amounts of the serum of that species of animal to be employed, thus enabling the bacteria to survive for a greater length of time after introduction into those animals.